Examining stigma, social support, and gender differences in unsuppressed HIV viral load among participants in HPTN 065

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Abstract Successful navigation of the HIV care continuum is necessary to maintain viral suppression. We explored gender-stratified correlates of being virally unsuppressed in the Prevention for Positives (P4P) component of HPTN 065. The outcome of interest was unsuppressed viral load (>40 copies/mL) among individuals already living with HIV. Correlates included medication adherence factors, social support and stigma. Logistic regression models were stratified by gender (N=673). Men-specific correlates of being virally unsuppressed included opposite-sex partners, older age and HIV disclosure stigma. Women-specific correlates included time since diagnosis, and personal-level barriers to medication adherence. When more individuals knew about their HIV status, women had over twice the likelihood of being virally unsuppressed; no such association was seen among men. Additionally, higher levels of social support were not associated with viral suppression among women. Interventions should consider gender-specific approaches to engaging social support in de-stigmatization of HIV and promotion of medication adherence and subsequent viral suppression.

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Introduction

In order to advance efforts to control HIV in the United States in line with the 'Ending the HIV Epidemic' plan, all persons living with HIV need timely linkage to care and successful long-term maintenance of medication adherence and viral suppression (United States Department of Health and Human Services 2019; Crepaz et al. 2016; Horn et al. 2016). However, many challenges exist in navigating this continuum. The impact of race and gender as barriers to navigating the care continuum are formidable, and related inequities in access have persisted since the beginning of the epidemic (Centers for Disease Control and Prevention (CDC) 2019; Crepaz et al. 2016; Horn et al. 2016). African Americans comprise less than 15% of the U.S. population but account for nearly half of new HIV diagnoses (CDC 2019, 2017).

Although the number of new HIV diagnoses have decreased among African American women, they remain more likely to experience treatment failure and be virally unsuppressed compared to women of other racial groups and compared to their African American male counterparts (CDC 2017,2019). Targeted research and interventions for effective rollout of the national 'Ending the HIV Epidemic: A Plan for America' must address these contextual issues (United States Department of Health and Human Services 2019; Lichtenstein et al. 2002; Turan et al. 2016).

Within the context of race and gender differences in viral suppression outcomes, social relationships and HIV stigma can have a great impact (Derlega et al. 2003; Li et al. 2008; Robinson and Knowlton 2016). Sensitive interaction



systems theory (SIST) has been used to better understand the variable effects of support from social relationships, including likelihood of receiving support, and costs of accessing support (whether instrumental, informational, or emotional; Lichtenstein et al. 2002; Cortopassi et al. 2019; Derlega et al. 2003). Central to SIST is interactive coping, a concept which describes provision and receipt of HIV care as a potential strain on the social relationship (Derlega et al. 2003). This occurs when care is not mutually agreed upon and recognized between caregivers and recipients, for example when social support is required of loved ones who lack skills or motivation to do so (Derlega et al. 2003; Li et al. 2008; Robinson and Knowlton 2016). This phenomenon may help to explain why African American women are at higher risk of treatment interruptions and faster AIDS progression than men, since they are more likely to provide support than to receive it (Cortopassi et al., 2019; Derlega et al. 2003; Maragh-Bass et al. 2020). Women, regardless of HIV status, are also more likely than men to provide unpaid care and have fewer financial resources to access care, thereby reinforcing interactive coping strain, stagnating care progression, and ultimately increasing likelihood of being virally unsuppressed (Robinson and Knowlton 2016; Rueda et al. 2016; Lichtenstein et al. 2002; Turan et al. 2016).

HIV stigma often arises from moral judgments placed on PLWH (Fullilove and Fullilove 1999; Bluthenthal et al. 2012). An HIV diagnosis may result in internalized stigma among persons living with HIV (PLWH), and PLWH often report feeling isolated and experiencing mental health challenges as a result of their HIV diagnosis (Payán et al. 2019; Turan et al. 2016). Stigma from disclosure to loved ones may result in alienation and relationship strain in racial minority communities, partly due to religious values (Fullilove and Fullilove 1999; Bluthenthal et al. 2012). Social ties strained by HIV stigma may result in care disruptions and greater risk of being virally unsuppressed, regardless of race, income, sexual orientation, and/or gender identity (Derlega et al. 2003; Barbee and Cunningham 1995). However, PLWH who have minority identities defined by race, sexual orientation, and/or gender identities face compounded stigma compared to their counterparts without these identities, and these intersectional stigmatized identities have also been shown to be associated with poor HIV-related health outcomes (Spieldenner 2016; Sutton and Parks 2013; Logieet al. 2011).

Our recent qualitative study of low-income, predominantly African American PLWH utilized SIST to examine the interrelationship of gender, social ties, stigma and health outcomes (Maragh-Bass et al. 2020). Analyses from 73 exit interviews conducted in a sub-study of the HIV Prevention Trials Network (HPTN 065) explored participants' lived experiences of HIV medication adherence and their views on the acceptability of financial incentives to promote viral suppression (Gamble et al. 2017; El-Sadr et al. 2017; Tolley et al. 2018; Greene et al. 2017). Our findings suggest that stigma due to HIV diagnosis and disclosure was experienced across several stages of adherence, and that women may experience and perpetuate HIV stigma more than men (Maragh-Bass et al. 2020). Finally, misaligned receipt and provision of support (e.g., strained interactive coping) can contextualize why women perceived less supportive ties despite identifying more social ties than men in our study (Maragh-Bass et al. 2020; Houston et al. 2015; Derlega et al. 2003).

Purpose

In order to better understand gender differences in HIV viral suppression outcomes, we examined correlates of being virally unsuppressed among participants in a subcomponent of HIV Prevention Trials Network, HPTN 065 study, a testing and linkage-to-care community-based trial with a cohort of predominantly African American participants. Specific aims were to explore: (a) associations between being virally unsuppressed, HIV stigma and social ties; and (b) gender differences in these associations.

Methods

Procedure

The present research utilized baseline data from the Prevention for Positives (P4P) component of the HPTN 065 study (Gamble et al. 2017; El-Sadr et al. 2017; McKinstry et al. 2017). Completed in 2015, this trial consisted of five interconnected study components conducted at clinics in Bronx, New York and Washington, D.C. (Gamble et al. 2017; El-Sadr et al. 2017; Tolley et al. 2018; Greene et al. 2017). The prevention for positives (P4P) study component evaluated the effect of a computerized prevention intervention (CARE +), designed to reduce behavioral risk factors such as unprotected sex among PLWH at 11 clinic sites. Participants (N = 937) were aged 18 and older, diagnosed with HIV, on antiretroviral therapy, and already receiving care at the participating clinics.

Measures

Dependent variable

The outcome of interest was detectable viral load (being virally unsuppressed), defined as viral load greater than 40 copies per mL/blood, where 0=suppressed viral load, versus

1 = unsuppressed viral load based on CDC guidelines for detectable viral load during the period in which the study was conducted (2011–2015; Centers for Disease Control and Prevention [CDC], n.d.).

Independent variables

The following variables were evaluated in relation to being virally unsuppressed: (a) socio-demographic factors: gender, race/ethnicity, education, age, income and type of sexual partners; (b) HIV treatment medication adherence factors: time since HIV diagnosis, medication adherence stage-of-change, personal-level barriers to medication adherence; (c) social relationship factors: who in social life knows about HIV, satisfaction with family support; and (d) HIV stigma factors: disclosure stigma, diagnosis stigma. Gender was measured via, "Are you:" where 0=Male, 1=Female, and 2=Transgender. Sexual partners were assessed via, "Do you have sex with:" where 0=Men, 1=Women, 2=Both men and women.

Socio-demographic factors Using responses to participants' gender and the gender of their sexual partners, a categorical variable was created, such that 0 = Men sexual partners only, 1 = Women sexual partners only, 2 = Both men and women sexual partners. This variable was used as a proxy for sexual orientation, which is interpreted differently by gender, e.g., 0 = homosexual among men but 0 = heterosexual for women. Race was assessed via a single question with a "check all that apply" option with the following racial categories: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Pacific Islander, White, Other Racial Background. Responses were collapsed, where 0 = African American or Black, 1 = White, 2 = Other race/Multiple races.

Participants were asked a separate binary question regarding Hispanic ethnicity, where 0 = Not Hispanic, and 1 = Hispanic. Education was assessed via, "What's the highest education you have finished?" Responses were collapsed, such that 0 = 8th grade or less/some high school, 1 = High school diploma/GED equivalent, 2 = Associate, technical, vocational degree, and 3 = Bachelor's degree/Graduate degree. Age was assessed as a continuous variable, with "How old are you," and was categorized such that 0 = 18 to 39 years, 1 = 40 to 49 years, 2 = 50 to 59 years, 3 = 60 years or older. Participants were asked to report their yearly household income. Categories were collapsed such that 0 = less than \$10,000, 1 = \$10,000 to \$19,999, 2 = \$20,000 to \$39,999,3 = \$40,000 to \$69,999, 4 = \$70,000 or more.

HIV medication adherence factors Time since HIV diagnosis was assessed via "how long ago did you find out you have HIV?" Participants entered numeric responses that

were categorized by year, such that 0 = less than 5 years since diagnosis, 1=5 to 9 years since diagnosis, 2=10 to 14 years since diagnosis, 3 = 15 to 19 year since diagnosis, 4=20 or more years since diagnosis. Medication stageof-change was assessed via, "People think a lot of things about taking their HIV meds. When you have thought about taking your HIV meds, which one of these statements best describe you?" Responses were on a 6-point Likert scale, ranging from 0 (I don't see any need to take my HIV medication every day) to 5 (I've been taking my HIV medication every day at the right times for the last 6 months) that corresponded to stages-of-change theory (e.g., Precontemplation, Maintenance; Genberg et al., 2013; Tolley et al. 2018; Greene et al. 2017). A sixth category was created in the event that respondents were not stageable or did not wish to respond; none of the respondents provided this response in surveys. Therefore, categories were collapsed such that 0 = Low-adherers (Stages 0 to 1), 1 = Action (Stages 2 to 4), 2 = Maintenance (Stage 5).

Next, participants were asked a series of 11 questions regarding barriers to medication adherence that they experienced. Items included "I simply forget to take my medications", and "I am embarrassed to take doses in front of others." Responses to each item were binary (yes/no) and summed to create an index of personal barriers to medication adherence that ranged from 0 to 10. A categorical variable was then created from the summed "barriers to medication" index score, where 0 = no barriers identified, 1 = 1 barrier identified, 2 = 2 barriers identified, and 3 = 3or more barriers identified. This variable was included for theoretical significance, based on our previous investigation of qualitative data with HPTN 065 sub-study participants (Tolley et al. 2018; Maragh-Bass et al. 2020). Findings suggested personal motivators and barriers to medication adherence differ among participants in Low-adherer and Action phases compared to Maintenance phases (Tolley et al. 2018; Maragh-Bass et al. 2020). Additionally, this index was created based on literature suggesting that increased barriers to medication adherence may be additive in effect, where a greater number may be associated with higher likelihood of non-adherence and being virally unsuppressed (Blashill et al. 2015; Robinson et al. 2016; Gray et al. 2011).

Social support factors Responses to "Who in your life knows about your HIV status?" were on a 4-point Likert scale, ranging from 0 (no one) to 4 (everyone). Satisfaction with family support was assessed with a single item that asked, "How satisfied are you with the support that you receive from your family?" Responses were on a 4-point Likert scale ranging from 0 (not satisfied) to 4 (very satisfied).

HIV stigma factors Stigma due to HIV diagnosis was assessed via a single item that asked whether individuals did not disclose their status because they did not want to think about the fact that they had HIV; responses were binary (yes/no). Next, participants were asked a series of 8 questions regarding reasons they did not disclose their HIV status to partners. Items included "I fear I'll be rejected by a partner if I disclose", "I can't talk about it in a public place" and "It's the partner's responsibility to ask me." Responses were binary (yes/no) and summed to create an index of "HIV stigma-related non-disclosure"; the index ranged from 0 to 8. Due to response distribution, a categorical variable was created where 0 = no types of stigma experiences identified, 1 = 1 type of experience identified, 2 = 2 types identified, and 3 = 3 or more types identified.

This index was created based on review of the literature suggesting that increased levels of stigma experienced when disclosing to social ties such as sexual partners may result in lower likelihood of disclosure, viral suppression, and medication adherence (Florom-Smith and Santis 2012; Blashill et al. 2015; Arnold et al. 2014). Inclusion of multiple dimensions of stigma was informed by existing literature and our analyses in HPTN 065 (Katz et al. 2013; Livingston and Boyd 2010; Maragh-Bass et al. 2020).

Analyses

Univariate frequencies were generated for dependent and independent variables on the total sample (N=937). Exploratory and confirmatory factor analyses were conducted on the two indices (barriers to medication adherence and HIV stigma-related non-disclosure), based on theoretical importance (Brown 2002; Tavakol and Dennick, 2011; Rao 1996). Both indices achieved one-factor solutions with acceptable fit using Cronbach's alpha (personal barriers to medication adherence: $\alpha = 0.69$, and HIV disclosure stigma ($\alpha = 0.70$ Brown 2002; Tavakol and Dennick 2011; Rao 1996). Next, bivariate statistics were calculated on variables of interest, and variables at least marginally significant (p < .10) were entered into a multiple logistic regression model (Gordon 2014; Long 1997). Bivariate and adjusted analyses with all predictor variables were stratified by gender due to hypothesized significance; individuals who identified as transgender were excluded due to small sample size (N = 14). Sexual orientation, race, satisfaction with family support, and HIV stigma variables were retained as control variables in the final model despite non-significance due to theoretical importance. Variable selection, including use of marginal significance in final models, was informed by SIST; constructs of interest were identified in previously described qualitative results (Maragh-Bass et al. 2020). Acceptable model fit was attained via goodness-of-fit tests for both the men-only ($\chi^2 = 4.98$; p > .05) and women-only models ($\chi^2 = 5.57$; p > .05); Hosmer and Lemeshow 2000).

After running regression models, marginal effects were calculated to inform how a dependent variable (outcome) changes when a specific independent variable (explanatory variable) changes (Gordon 2014; Long 1997). Other covariates were assumed to be held constant. Marginal effects are often calculated as a partial derivative and can be useful when analyzing regression analysis results. They were calculated to (a) compare relationships across genders, rather than within gender as in the regression models; and (b) explore stigma and social factors as informed by our previous qualitative analyses of HPTN 065 sub-study data. While the full sample size utilized in univariate statistics was N = 937 (Table 1), the final sample size in the regression models was N = 637 (Table 2), due to missing data across variables. Quantitative analyses were conducted on complete cases only due to acceptable missingness (≤ 10 percent missingness per variable; Bennett 2001). Robust standard errors were used for two purposes: first, to account for wide dispersion in the data (Long 1997). Second, robust standard errors utilize full information maximum likelihood parameters for estimation, which asymptotically equivalent to multiple imputation and is best for addressing data missingness when data are missing not completely at random as was the case in the present sample (Shin et al. 2017; Long 1997; Dong and Peng 2013). Analyses were run in STATA Version 14.0 (StataCorp 2015).

Results

Study participants

Table 1 reports socio-demographic characteristics for all study participants. Participants were predominantly men (69.8%), African American (63.9%), and non-Hispanic (79.7%). Roughly half of participants had a yearly income under \$20,000 (47.1%), were over the age of 50 (57.1%) and had a high school diploma equivalent or less education (57.3%). Regarding gender differences in socio-demographics, women were significantly more likely than men to have less than a high school education (30.4% vs. 13.3%, p < .001). Women were also significantly more likely to identify only opposite-sex partners (86.4% vs. 38.5%; p < .001) and identify Hispanic ethnicity (27.7% vs. 17.2%; p < .001). While women were more likely to identify at least one experience of stigma related to HIV disclosure (41.4% vs. 29.2%; p < .001), men were more likely to identify 3 or more experiences related to HIV disclosure stigma (22.7% vs. 13.1%; *p* < .001).

Characteristic	Men $(n = 654) \%$ (n)	Women ($n = 283$) %(n)	Total (<i>N</i> =937) % (<i>N</i>) or Mean (SD)	
Sexual partners identified***				
Men only	54.0 (341)	78.4 (222)	37.9 (355)	
Women only	38.5 (243)	5.5 (14)	49.6 (465)	
Both men and women	7.5 (47)	7.4 (21)	7.3 (68)	
Race ^{***}				
African American/Black	62.9 (410)	66.2 (186)	63.9 (596)	
White	17.5 (114)	5.0 (14)	13.7 (128)	
Asian/American Indian/Other	19.6 (128)	28.8 (81)	22.4 (209)	
Hispanic ethnicity ^{***}				
No	82.8 (540)	72.3 (204)	79.7 (744)	
Yes	17.2 (112)	27.7 (78)	20.3 (190)	
Age [*]				
18–39 years	14.3 (93)	16.0 (45)	14.8 (138)	
40–49 years	25.8 (168)	33.6 (94)	28.1 (262)	
50–59 years	40.8 (266)	37.5 (105)	39.8 (371)	
60 + years	19.1 (125)	12.9 (36)	17.3 (161)	
Education***			. /	
8th grade or less/Some high school	13.3 (87)	30.4 (86)	18.4 (173)	
High school diploma/GED	36.4 (238)	44.5 (126)	38.9 (364)	
Technical/Associate degree	19.7 (129)	12.7 (36)	17.6 (165)	
Bachelor/Graduate degree	30.6 (200)	12.4 (35)	25.1 (235)	
Yearly income ^{***}				
≤\$10,000	22.5 (147)	41.3 (117)	28.2 (264)	
\$10,000-\$19,999	19.1 (125)	18.4 (52)	18.9 (177)	
\$20,000-\$39,999	17.0 (111)	17.7 (50)	17.2 (161)	
\$40,000-\$69,999	18.2 (119)	6.7 (19)	14.7 (138)	
\$70,000 +	23.2 (152)	15.9 (45)	21.0 (197)	
Viral load				
Suppressed	77.8 (505)	74.7 (210)	76.9 (715)	
Unsuppressed	22.2 (144)	25.3 (71)	23.1 (215)	
Fime since HIV diagnosis				
≤ 5 years	18.9 (124)	17.0 (48)	18.4 (172)	
5–9 years	13.9 (91)	13.4 (38)	13.8 (129)	
10–14 years	14.7 (96)	18.4 (52)	15.8 (148)	
15–19 years	15.1 (99)	19.8 (56)	16.5 (155)	
20 + years	37.3 (244)	31.4 (89)	35.5 (333)	
Who in life knows about HIV status			0000 (000)	
No one	5.1 (33)	5.4 (15)	5.2 (48)	
A few people	63.8 (413)	60.4 (169)	62.8 (582)	
A lot of people	21.0 (136)	22.1 (62)	21.4 (198)	
Everyone	10.1 (65)	12.1 (34)	10.7 (99)	
Satisfaction with family support	10.1 (03)	12.1 (51)	10.7 (57)	
Not satisfied	49.4 (311)	54.3 (151)	50.9 (462)	
Somewhat satisfied	42.3 (266)	35.9 (100)	40.4 (366)	
Satisfied	5.7 (36)	6.1 (17)	5.8 (53)	
Very satisfied	2.5 (16)	3.6 (10)	5.8 (53) 2.9 (26)	
Adherence stages-of-change	2.5 (10)	5.0 (10)	2.7 (20)	
Low-adherers	23.5 (134)	19.7 (40)	22.5 (174)	
Action	47.1 (268)	51.7 (105)	48.3 (373)	

Table 1 (continued)

Characteristic	Men $(n = 654) \%$ (n)	Women ($n = 283$) %(n)	Total ($N = 937$) % (N) or Mean (SD)	
Maintenance	29.4 (167)	28.6 (58)	29.2 (225)	
Personal barriers to adherence ⁺				
0 barriers identified	49.3 (286)	55.7 (127)	51.1 (413)	
1 barrier	26.4 (153)	18.4 (42)	24.1 (195)	
2+ barriers identified	24.3 (141)	25.9 (59)	24.8 (200)	
HIV stigma disclosure experiences***				
0 experiences identified	31.5 (197)	28.7 (77)	30.7 (274)	
1 type of experience identified	29.2 (183)	41.4 (111)	32.9 (294)	
2 types of experiences identified	16.6 (104)	16.8 (45)	16.7 (149)	
3 + of experiences identified	22.7 (142)	13.1 (35)	19.8 (177)	
HIV stigma related to diagnosis				
No	88.8 (556)	88.8 (238)	88.8 (794)	
Yes	11.2 (70)	11.2 (30)	11.2 (100)	

[§]Some variables do not total 100% due to missing data

Significant or marginally significant gender differences (χ^2) at: ${}^{\dagger}p < .10$, ${}^{*}p < .05$, ${}^{**}p < .01$, ${}^{***}p < .001$

Logistic regression results: men

Adjusted analyses are shown in Table 2 and Fig. 1. Factors associated with increased likelihood of being virally unsuppressed among men included having greater personal-level barriers to adherence and having identified opposite-sex partners only. Factors associated with decreased likelihood of being virally unsuppressed included time since diagnosis and age. Men who identified opposite-sex partners had over twice the likelihood of being virally unsuppressed than men who identified only same-sex partners [Adjusted Odds Ratio (AOR) = 2.12; 95% Confidence Interval (95%) CI) = 1.17, 3.86; p < .01]. Compared to Hispanic men, non-Hispanic men had a significantly higher association with being virally unsuppressed (Hispanic men: AOR = 0.33; 95% CI = 0.13, 0.82; p < .05). Compared to men with less than a high school education, more education was associated with less likelihood of being virally unsuppressed (AOR = 0.39; 95% CI=0.16, 0.99; p < .05). Compared to men who were diagnosed more than 15 years ago, men who had been diagnosed in the prior five years had higher likelihood of being virally unsuppressed (Men with 15 to 19 years since diagnosis: AOR = 0.40; 95% CI = 0.17, 0.90; *p* < .05). Finally, men who identified multiple personal-level barriers to adherence had nearly twice likelihood of being virally unsuppressed as men who did not identify any personal-level barriers to medication adherence (AOR = 2.00; 95% CI = 1.08, 3.70; p < .05).

Logistic regression results: women

As shown in Fig. 1, factors associated with increased likelihood of being virally unsuppressed among women included personal-level barriers to adherence, education, and who in their lives knew their HIV status. Factors associated with decreased likelihood of being virally unsuppressed included time since HIV diagnosis and having identified both same and opposite-sex partners. Compared to women who identified opposite-sex only partners, women who identified both types of sex partners had lower association with being virally unsuppressed (AOR = 0.10; 95% CI = 0.01, 1.05; p < .10). Compared to women who were diagnosed less than 5 years prior to study participation, women who had been diagnosed more than 20 years ago had much lower association with being virally unsuppressed (AOR = 0.18; 95% CI = 0.05, 0.62; p < .01). Compared to women who did not identify any personal-level barriers to medication adherence, women who identified one barrier had 3 times higher of an association with being virally unsuppressed (AOR = 3.36; 95% CI = 0.94, 11.95; p < .05). Women who identified two or more personal-level barriers to medication adherence had nearly fivefold higher association with being virally unsuppressed compared to women who identified no barriers (AOR = 4.77; 95% CI = 1.77, 12.87; p < .01). Finally, each addition in the number of individuals who knew about a woman's HIV status was associated with more than twofold greater association with being virally unsuppressed (AOR = 2.59; 95% CI = 1.38; 4.87; p < .001).

	Men (N=490)			Women (N=183)				
	UOR ^a	CI ^c	AOR ^b	CI	UOR	CI	AOR	CI
Sexual partners								
Ref: Men only	1.00		1.00		1.00		1.00	
Women only	1.20	(0.81, 1.77)	2.12**	(1.17, 3.86)	1.76	(0.55, 5.60)	0.46	(0.12, 1.80)
Both men and women	0.98	(0.47, 2.07)	1.84	(0.76, 4.44)	0.66	(0.21, 2.05)	0.10*	(0.01, 1.05)
Race/ethnicity	0120	(0117, 2107)	1101	(01/0, 111)	0.00	(0.21, 2.00)	0110	(0.01, 1.00)
Ref: African American/Black	1.00		1.00		1.00		1.00	
White	0.56*	(0.32, 0.98)	0.56	(0.24, 1.31)	0.87	(0.23, 3.26)	1.93	(0.22, 17.01)
Other	0.98	(0.52, 0.93) (0.62, 1.57)	1.57	(0.24, 1.51) (0.75, 3.26)	1.26	(0.23, 3.20) (0.70, 2.28)	0.69	(0.22, 17.01)
Hispanic	0.90	(0.02, 1.57)	1.57	(0.75, 5.20)	1.20	(0.70, 2.20)	0.09	
Ref: No	1.00		1.00		1.00		1.00	(0.16, 2.96)
Yes	0.72	(0.43, 1.22)	0.33*	(0.13, 0.82)	1.34	(0.75, 2.41)	2.51	(0.10, 2.90) (0.49, 12.84)
	0.72	(0.43, 1.22)	0.55	(0.13, 0.82)	1.54	(0.73, 2.41)	2.51	(0.49, 12.84)
Age	1.00		1.00		1.00		1.00	
Ref: 18–39 years	1.00	(0.40.4.40)	1.00		1.00	(0.07.1.(0))	1.00	
40–49 years	0.84	(0.48, 1.46)	1.32	(0.62, 2.82)	0.79	(0.37, 1.69)	0.87	(0.27, 2.87)
50–59 years	0.51**	(0.30, 0.86)	0.77	(0.36, 1.65)	0.51*	(0.24, 1.09)	0.38	(0.11, 1.30)
60 + years	0.26***	(0.13, 0.53)	0.39*	(0.13, 1.13)	0.23*	(0.07, 0.76)	0.27	(0.04, 1.83)
Education								
Ref: < 8th grade/Some high school	1.00		1.00		1.00		1.00	
High school diploma/GED	0.57*	(0.33, 0.98)	0.53	(0.23, 1.21)	1.13	(0.61, 2.10)	2.22 [*]	(0.84, 5.90)
Technical degree	0.47^{*}	(0.25, 0.88)	0.47^{*}	(0.19, 1.17)	0.65	(0.25, 1.69)	1.45	(0.37, 5.66)
Some college or more	0.43**	(0.24, 0.76)	0.39*	(0.16, 0.99)	0.35 [‡]	(0.11, 1.10)	1.96	(0.42, 9.18)
Time since HIV diagnosis								
Ref: \leq 5 years	1.00		1.00		1.00		1.00	
5–9 years	0.66	(0.35, 1.22)	0.30**	(0.13, 0.71)	0.60	(0.23, 1.51)	0.24^{*}	(0.05, 1.22)
10-14 years	0.68	(0.37, 1.24)	0.38^{*}	(0.17, 0.83)	0.46^{*}	(0.19, 1.11)	0.15^{*}	(0.03, 0.72)
15–19 years	0.52^{*}	(0.28, 0.97)	0.40^{*}	(0.17, 0.90)	0.36^{*}	(0.15, 0.89)	0.15^{**}	(0.04, 0.60)
20 + years	0.45**	(0.27, 0.75)	0.30***	(0.15, 0.59)	0.56	(0.26, 1.19)	0.18^{**}	(0.05, 0.62)
Family support satisfaction								
Ref: not satisfied	1.00		1.00		1.00		1.00	
Somewhat satisfied	1.04	(0.70, 1.54)	1.11	(0.66, 1.87)	1.56	(0.88, 2.76)	1.27	(0.50, 3.23)
Satisfied	1.16	(0.52, 2.58)	0.76	(0.27, 2.14)	1.42	(0.47, 4.33)	0.61	(0.10, 3.75)
Very satisfied	0.54	(0.12, 2.43)	0.30	(0.03, 2.68)	0.38	(0.05, 3.11)	1.54	(0.15, 15.40)
Adherence stage								
Ref: Low-adherer	1.00		1.00		1.00		1.00	
Action	1.27	(0.75, 2.17)	1.09	(0.59, 2.01)	0.77	(0.31, 1.89)	0.99	(0.32, 3.04)
Maintenance	1.22	(0.69, 2.18)	0.97	(0.47, 2.02)	1.20	(0.47, 3.10)	1.28	(0.37, 4.47)
Personal-level adherence barriers		(0.027, 2.2.0)		(0111, 2102)		(0111,0110)		(0.0.1, 1.1.)
Ref: 0 barriers identified	1.00		1.00		1.00		1.00	
1 barrier identified	1.49	(1.32, 3.50)	1.20	(0.67, 2.17)	1.33	(0.53, 3.30)	3.36 [‡]	(0.94, 11.95)
2+ barriers identified	2.15**	(0.90, 2.47)	2.00*	(1.08, 3.70)	2.68**	(1.28, 5.57)	4.77 ^{**}	(1.77, 12.87)
HIV disclosure stigma experiences	2.15	(0.90, 2.17)	2.00	(1.00, 5.70)	2.00	(1.20, 5.57)	,	(1.77, 12.07)
Ref: 0 experiences identified	1.00		1.00		1.00		1.00	
1 type of experience	0.77	(0.46, 1.28)	0.58 ⁺	(0.31, 1.10)	1.63	(0.79, 3.35)	1.60	(0.60, 4.38)
	1.57 ⁺			(0.31, 1.10) (0.75, 3.04)		(0.79, 3.35) (0.68, 3.95)		(0.00, 4.38) (0.29, 6.44)
2 types of experiences identified 3+ types of experiences identified	0.87	(0.92, 2.68)	1.51 0.53	,	1.64		1.38	,
•• •	0.87	(0.51, 1.48)	0.55	(0.23, 1.21)	2.06	(0.82, 5.18)	1.39	(0.27, 7.01)
HIV diagnosis stigma experiences	1.00		1.00		1.00		1.00	
Ref: No	1.00	(0.70, 1.71)	1.00	(0.45.0.50)	1.00	(0.50. 0.11)	1.00	(0.20. 5.(5)
Yes	1.16	(0.79, 1.71)	1.12	(0.45, 2.76)	1.35	(0.58, 3.11)	1.48	(0.39, 5.63)
Who know HIV status (continuous)	1.02	(0.79, 1.31)	1.17	(0.79, 1.73)	1.18	(0.83, 1.67)	2.59^{**}	(1.38, 4.87)

 ^{+}p < .10, $^{*}p$ < .05, $^{**}p$ < .01, $^{***}p$ < .001

^aUOR = Unadjusted Odds Ratio, ^bAOR = Adjusted Odds Ratio (for all other variables in model), ^cCI = 95% confidence interval

	Association with likelihood of being virally unsuppressed			
Variables	Men	Women		
being virally	Personal-level barriers to medication adherence Opposite sex partners	Personal -level barriers to medication adherence Education Who in life knows about HIV status		
Factors which being virally unsuppressed	Time since diagnosis Age	Time since diagnosis Same and opposite sex partners		

Fig. 1 Factors associated with being virally unsuppressed by gender*. *Includes marginally significant findings at (p < .10)

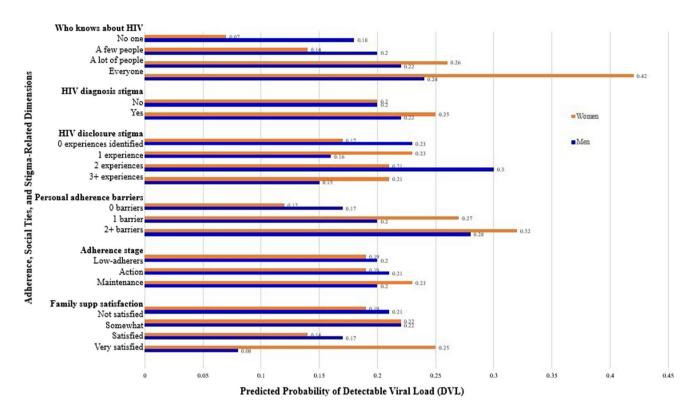


Fig. 2 Predicted probability of being virally unsuppressed exploring stigma and social factors by gender (marginal effects)

Marginal effects: gender differences in social ties and stigma

Social ties, stigma, and gender were all identified as potential correlates of medication adherence and viral suppression in our previous qualitative analyses, which we explored further in the larger quantitative sample of HPTN 065 P4P participants (Fig. 2). Marginal effects of the predicted probability of being virally unsuppressed were calculated holding the other covariates constant, to assess the relationship between being virally unsuppressed, medication adherence factors and social factors by gender (Fig. 2). The association between HIV diagnosis stigma and adherence stage of change on being virally unsuppressed were similar for men and women. However, compared to men, women had a higher predicted probability of being virally unsuppressed when everyone in their social life knew

about their HIV status (0.42 vs. 0.24). Compared to women who identified one experience of HIV stigma disclosure, men who identified one experience had a higher predicted probability of being virally unsuppressed (0.30 vs. 0.21). Lastly, women who were not satisfied with the support they received from family had a much higher predicted probability of being virally unsuppressed than men who were not satisfied with the support received from family (0.25 vs. 0.08).

Discussion

In this study, we explored associations between social relationships, stigma and being virally unsuppressed among participants in HPTN 065 on antiretroviral therapy. Nearly onefourth of participants were virally unsuppressed (23.1%). Viral suppression has been shown to be associated with CD4 + cell count recovery, decrease in HIV-related complications, better survival and decreases in HIV transmission, highlighting the need for research to identify factors which can reduce likelihood of being virally unsuppressed (Friedman et al. 2015; Risher et al. 2015; Cohen et al. 2011; Rodger et al. 2016; Bavinton et al. 2018).

Reporting two or more personal-level barriers to medication adherence were associated with greater likelihood of being virally unsuppressed among both men and women. In the present study, this index was developed based on previous literature which suggests there may be an additive effect of barrier to adherence on likelihood of being virally unsuppressed (Blashill et al. 2015; Robinson et al. 2016; Gray et al. 2011). This suggests that while genderbased interventions to support viral suppression are wellfounded (Pellowski et al. 2018; Haberland 2015; Robinson and Knowlton 2016), approaches must be cognizant of the needs of those who have access to HIV care yet still experience negative health outcomes such as being virally unsuppressed irrespective of gender. This index also builds on previous research by Highstein et al. (2006), that found that weighing pros and cons of medications (i.e., decisional balance) combined with stage of readiness for medication adherence at baseline positively predicted viral load at one year follow-up among a predominantly African American cohort of women. Informed by Highstein et al. (2006), future studies of personal-level barriers using this type of index should explore resiliencies which are salient for overcoming these types of barriers. These might include resilience or hope for a long life, which was a sentiment described in our qualitative study of HPTN 065 (Maragh-Bass et al. 2020).

Also, among both genders, we found lower likelihood of being virally unsuppressed for individuals over the age of 60. While it is possible that the reason for this is greater time since HIV diagnosis, future research should explore age-related differences in being virally unsuppressed along with time since HIV diagnosis and continuous engagement in care. Barriers to care engagement among those living with HIV over ten years may include care disruptions and increased negative care experiences. They may also be experiencing co-morbid illnesses such as substance use and mental illness, the rates of which increase in older minority populations living with HIV who have seen decades of changes in HIV treatment (Robinson et al. 2016; Fang et al. 2015; Emlet et al. 2015).

Men-specific correlates of being virally unsuppressed included opposite-sex partners, and HIV disclosure stigma. Women-specific correlates included time since HIV diagnosis, and personal-level medication adherence barriers. Many of these individuals had been living with HIV over ten years, and research generally suggests that that longer the time since diagnosis, the higher the likelihood of achieving and maintaining viral suppression. Our results suggest that facilitation of HIV medication adherence is urgently needed, even among individuals who have been diagnosed and in care for longer periods of time.

In adjusted analyses, men who identified only oppositesex partners had higher associations with being virally unsuppressed compared to men who identified same-sex only partners which we did not find with women. Existing literature suggest that men with same-sex partners have both higher rates of HIV infection and may also have lower rates of viral suppression than their heterosexual male counterparts (Fleming et al. 2016; Hall et al. 2013; Higging et al. 2013). Post-hoc analyses did not reveal differences in personal-level barriers to medication adherence among men by sexual partners identified; therefore, more research is needed to identify protective factors to promote viral suppression in this population considering factors such as sexual orientation within and by gender identity.

While only marginally statistically significant, women who identified both same-sex and opposite-sex partners had a 90% lower association with being virally unsuppressed than women with only opposite-sex partners (p < .10). Few studies have evaluated the association between sexual partners and likelihood of viral suppression among women PLWH, particularly those who identify as lesbian, bisexual or queer. It is possible that women who identify other than heterosexual may have lower likelihood of being virally unsuppressed because they may openly discuss HIV, sexuality, and supportive care needs; however, due to the sample size in the present study these findings must be interpreted with caution. Nonetheless, Logie et al. (2011) found that women who identify as bisexual may not maintain safer sex self-efficacy, social support, and community connectedness over time after their HIV/STI intervention. Coupled with study findings, this suggests the need for longitudinal evaluation of the role of sexual partners, sexual orientation, and facilitating viral suppression among women living with HIV (Logie et al. 2011).

While only marginally significant, men with an experience with HIV disclosure stigma had a greater association with being virally unsuppressed. This is consistent with the literature that reflects the deleterious effects of pervasive stigma on HIV-related health outcomes (Florom-Smith and Santis 2012; Blashill et al. 2015; Arnold et al. 2014; Livingston and Boyd 2010). However, this finding was not additive, i.e., men with more than three stigma disclosure experiences did not have greatest likelihood of being virally suppressed. It is possible that men with only one salient experience of disclosure stigma may have less likelihood of coping and mitigating the experience's effect on their viral suppression, as compared to those that have not experienced any stigma or those who constantly experience stigma. Next, post-hoc analyses show that Hispanic/Latino men reported fewer experiences of HIV disclosure stigma as compared to their non-Hispanic PLWH counterparts. Additionally, Hispanic/Latino ethnicity was associated with significantly lower likelihood of being virally unsuppressed among men. More research is needed to understand the day-to-day experiences of stigma that may impact personal-level behaviors such as medication adherence, including understanding nuances related to ethnicity and cultural perceptions of HIV stigma (Blashill et al. 2015; Arnold et al. 2014; Livingston and Boyd 2010).

Finally, similar to our prior qualitative study, gender differences were noted in the present analyses. Marginal effects, run after logistic regression models, showed that predicted probability of being virally unsuppressed was associated with dimensions of strained social interactions more frequently among woman than men (e.g., when more people knew their HIV status). It is possible that gender differences may explain more of the strained social support experienced, given that most of the sample is African American (i.e., the lack of association by race may be due to limited variation in race in the study sample). This association, therefore, must be interpreted cautiously due to intersectional challenges of racism and sexism that are well documented among African American women living with HIV (Fullilove and Fullilove 1999; Friedman et al. 2015; Robinson and Knowlton 2016).

Limitations

This study is subject to several limitations. First, analyses were informed by our previous HPTN 065 qualitative substudy, and sub-study participants may not fully represent participants who completed the larger HPTN 065 study. Similarly, the present regression and post-hoc analyses were cross-sectional and must be examined longitudinally to identify causal relationships between these and other variables of interest in adjusted analyses. Longitudinal analyses could help to illuminate complex associations such as that of experiences of disclosure stigma and likelihood of being virally unsuppressed; findings among men suggest there may be a trend though it may not be an additive effect. Secondary analyses were conducted on survey items and scales which may not fully capture gendered experiences related to HIV health outcomes and were not specifically developed for the present analyses of gender, stigma, social support, and HIV outcomes. For example, items related to personal-level barriers of medication adherence may not capture challenges such as child care and family obligations, which African American women are more likely than women of other groups to provide to both their children and grandchildren and which may impede care (Jemison et al. 2019; Feaster et al. 2010; Dunlap et al. 2006). Similarly, the association between the

number of individuals who knew one's HIV status and being virally unsuppressed may be related to stigma; however, the survey measures included in the present study did not focus on this nuance. Measurement error in survey items may prevent us from being able to parse gender norms and social desirability bias related to discussion of social support and HIV care needs. Third, the HPTN 065 study was conducted in Bronx NY and Washington, DC, with a predominantly African American and male population who were living with HIV for more than 10 years. The larger HPTN 065 did not over-recruit male participants by study design; therefore, it is possible that males are over-represented in the study sample because 40% of males in the full study sample contracted HIV through sex with other men and this population itself is over-represented among African Americans living with HIV. Consequently, analyses were stratified by gender due to theoretical importance, which may have led to a loss of statistical power to detect significant findings as evidence by wide confidence intervals particularly among the women-only results. Next, the present analyses are limited to self-identified men and women, and participants were not explicitly asked their sexual orientation.

Therefore, findings do not represent the experiences of non-binary individuals living with HIV, nor to the views or experiences of individuals who self-identify as sexual and gender minorities. Additionally, being virally unsuppressed was not associated with transmission mode in the present sample, therefore this association should be explored in future research. Similarly, rates of substance use and depressive symptoms in the present sample were low, and therefore excluded in present analyses but are relevant for exploration in future research.

Next, findings include marginally significant findings (p < .10); however, given the cross-sectional nature of data and the smaller sample size among stratified analyses, marginally significant findings are worth noting for implications for future research although they must be interpreted with caution (Pristschet et al. 2016). Finally, several measures including time since HIV diagnosis, medication adherence stage-of-change, and socio-demographic factors were identified with a single item; therefore, no factor analyses or reliability estimates were ascertained. However, inclusion of single items has been defended in previous research, namely because they may identify specific behavioral factors associated with outcomes of interest in a given study population (Rossiter 2008).

Conclusion

Despite limitations, our findings suggest that both men and women who experienced greater barriers to adherence had much higher odds of being virally unsuppressed. Women may experience a greater additive effect than men of personal-level barriers to medication adherence and strained social relationships as a result of their HIV status. Findings stress the importance of integrating the context of intersectional gender-based disadvantage, and HIV stigma and social relationships when designing interventions to promote viral suppression outcomes. Doing so will provide great impact toward 'ending the epidemic' in the US.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Human and animal rights and Informed consent All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All research participants completed informed consent forms that were fully approved by the IRB. Additionally, the authors have no disclosures of any kind to report.

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